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EXAMINER	
HOWARD, ZACHARY C	

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1646	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/542,408	ITO ET AL.	
	Examiner	Art Unit	
	ZACHARY C. HOWARD	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 November 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-58 and 67-77* is/are pending in the application.

4a) Of the above claim(s) *2,4-13,15-58,69 and 71-77* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,14,67,68 and 70* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-58 and 67-77* are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *15 July 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *7/15/05;9/19/06;11/23/09*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Application, Amendments and/or Claims

Claims 1-58 and 67-77 are pending in the instant application.

Election/Restrictions

Applicants' election without traverse of Group I, claims 1, 3, 14 and 67-70, in the reply filed on 11/23/09 is acknowledged.

Claims 2, 4-13, 15-58 and 71-77 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made without traverse in the reply filed on 11/23/09.

Applicants' election of the species of (1) SEQ ID NO: 1 (human) and (2) diabetes mellitus in the reply filed on 11/23/09 is acknowledged.

Claim 69 is withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species, there being no allowable generic or linking claim.

Claims 1, 3, 14, 67, 68 and 70 are under consideration, as they read upon the elected species.

Specification

The disclosure is objected to because of the following informalities:

(1) The title of the invention ("NOVEL SCREENING METHOD") is not descriptive, because it is not specific to the claimed invention, which is a method of screening using a GPCR that binds a fatty acid. A new title is required that is clearly indicative of the invention to which the claims are directed.

(2) An updated priority statement of the instant application's parent provisional and nonprovisional applications should be included in the first sentence of the specification or application data sheet. Specifically, the priority statement should indicate that the instant application is a 371 of PCT/JP04/00248, filed 1/15/2004.

Appropriate correction is required.

Claim Rejections - 35 USC § 112, 2nd paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 3, 14, 67, 68 and 70 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01.

In claim 1, the omitted steps are: method steps that indicate how the receptor protein and the fatty acid are used to a screen a compound that changes the binding property of the receptor and the fatty acid. Furthermore, the method steps fail to recite a step where the compound to be screened is used in the method. Independent claim 1 merely recites that a receptor protein and a fatty acid will be used without providing any steps that indicate how it will be used. Dependent claims 3 and 14 are included in this rejection for the same reasons as claim 1.

In claim 67, the omitted steps are: method steps that indicate how the receptor protein is to be used in an assay to confirm a drug for preventing/treating diabetes binds to a GPCR of SEQ ID NO: 1. Furthermore, the method steps fail to recite a step where the drug to be screened is used in the method. Dependent claims 68 and 70 are included in this rejection for the same reasons as claim 67.

Claims 1, 3, 14, 67, 68 and 70 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is indefinite because it is unclear what a "salt" of a receptor is. Salts, in chemistry, generally refer to neutralized acids (e.g., a salt of a fatty acid is understandable); however it is not clear how this is applied to a G-protein coupled receptor protein. The specification repeatedly uses this term but does not explain what is meant by it or structurally define a "salt" of a receptor. Each of claims 3, 14, 67, 68 and 70 is rejected for the same reason.

Claim 67 is also indefinite because the elements recited in the claim do not constitute a proper Markush group. The recitation of "preventing/treating" (line 2) is equivalent to "preventing and/or treating". The alternative use of “and/or” (or the equivalent) is indefinite because it is not clear what controls which of these limitations. See MPEP § 2173.05(h). Dependent claims 68 and 70 are indefinite for the same reason (claim 68 recites "preventing/treating" in line 2; claim 70 is included because it depends from rejected claim 67).

Claim 68 is also indefinite because it twice recites "a drug for preventing/treating" in line 2, and it is unclear how this duplicate recitation limits the claim.

Claim Rejections - 35 USC § 112, 1st paragraph, enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 3, 14, 67, 68 and 70 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for

A method of screening, or confirming that a drug binds to a receptor, comprising

(i) contacting *in vitro* a polypeptide comprising SEQ ID NO: 1 with a fatty acid in the presence of a test compound and determining (a) the binding of the fatty acid to the receptor, or (b) a cell-based activity stimulated by binding of the fatty acid to the receptor,

(ii) contacting *in vitro* a polypeptide comprising SEQ ID NO: 1 with a fatty acid in the absence of a test compound and determining (a) or (b), and

(iii) comparing the determinations made in steps (i) and (ii),

wherein a change in binding or cell-based activity in the presence of the test compound as compared to the absence of the absence of the test compound indicates that the test compound changes the binding between the fatty acid and the receptor, or changes the cell-based activity stimulated by binding of the fatty acid to the receptor,

does not reasonably provide enablement for

A method of screening as recited in claims 1, 3, or 14, or a method for confirming as recited in claims 67, 68 or 70 [*these claims have not been written out in full here due the length of each claim*].

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is “undue” include, but are not limited to: 1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability in the art, 5) existence of working examples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

The nature of the invention encompasses methods of screening using a G-protein coupled receptor of SEQ ID NO: 1. SEQ ID NO: 1 is designated "14273" in the specification, but is known in the relevant art as human GPR120 (see the record for GenBank Protein Database Accession Number AAIOO1176, titled "GPR120 protein [Home sapiens]", dated Oct 4, 2006, 1 page as printed; cited here solely as evidence of the amino acid sequence of GPR120). The claimed methods of screening involve the binding or agonist activity of a fatty acid to the receptor.

The specification provides the following working examples in support of the claimed invention. Example 1 is titled "Confirmation of the reactivity of fatty acids with human and mouse 14273", and shows that CHO-K1 cells expressing human or mouse GPR120 (by transfection) produced increased intracellular calcium in response to several long chain fatty acids including palmitoleic acid, linoleic acid, γ-linolenic acid, arachidonic acid and docosahexanoic acid. Example 2 describes the expression of human GPR120 mRNA including "that the mRNA was highly expressed in the hypophysis, adipose tissue and colon" (pg 132). Example 3 describes the expression of rat GPR120 mRNA, with high expression in similar tissues. Example 4 describes

cloning of the rat GPR120 gene. Example 5 describes the "Effects of fatty acids on cAMP production in human 14273-expressed CHO cells" (pg 133). Example 6 is titled "MAP kinase activation in human 14273-expressed CHO cells by addition of the fatty acid". Examples 7 and 8 are titled "Change in expression of the 14273 receptor accompanied by the induction of differentiation of" either "3T3-L1 cells into adipocytes" (Example 7) or "rat primary culture preadipocytes into adipocytes" (Example 8). These examples show an increase in expression of GPR120 that corresponds with cell differentiation into adipocytes. Example 9 is titled, "Activity of suppressing adrenocorticotropic hormone (ACTH)-secretion from AtT-20 cells by fatty acids". This example provides results showing that long chain fatty acids suppress ACTH secretion induced by CRF (corticoptropin-releasing factor) whereas short chain fatty acids (which are not agonists of GPR120) do not. Example 10 describes "Lipolysis suppressing action of a fatty acid in 3T3-L1 adipose differentiation cells". Example 11 describes "Suppressed expression of mouse 14273-GFP-fused protein by introducing siRNA specific to the sequence of mouse 14273" (pg 138).

The results of the working examples indicate that GPR120 is a receptor for long chain fatty acids (i.e., fatty acids with more that 12 carbons). These results are supported by publications in the relevant literature. For example, Tanaka et al (2008) teaches that GPR120 is a fatty acid receptor, and that interaction of fatty acid with GPR120 induces secretion of cholecystokinin, which "is important in digestion because it plays a key role in regulating a range of intestinal responses, which include stimulation of pancreatic secretion, gall bladder emptying, and inhibition of gastric motility … collectively, these responses help to integrate and optimize the digestion of fat" (pg 523 of Tanaka et al (2008. Naunyn-Schmiedeberg's Arch Pharmacol. 377:523-527).

The working examples in the specification and the relevant literature provide support for the use of the claimed method in identifying agonists or antagonists of the interaction between long chain fatty acids and the human GPR120 receptor of SEQ ID NO: 1. However, the specification fails to provide enablement for the following embodiments encompassed by the claims:

(1) The claims encompass methods of screening using "the same or substantially the same amino acid sequence as the amino acid sequence represented by SEQ ID NO: 1" or "its partial peptide".

The specification describes a large genus of mutations that can be made in SEQ ID NO: 1 (see paragraph 34 of the published application), but does not provide any guidance as to which amino acid substitutions, deletions or insertions to make to achieve any desired property, or defined a difference in structure, or difference in function, between proteins corresponding to SEQ ID NO: 1 and variants of said proteins. The claims do not place any structural or functional limitations on the proteins to be used.

The problem of predicting protein structure from sequence data and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein is extremely complex. While it is known that many amino acid substitutions are generally possible in any given protein, the positions within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of success are limited. Certain positions in the sequence are critical to the protein's structure/function relationship, e.g. such as various sites or regions directly involved in binding, activity and in providing the correct three-dimensional spatial orientation of binding and active sites. These regions can tolerate only relatively conservative substitutions or no substitutions [see Wells (18 September 1990) "Additivity of Mutational Effects in Proteins." Biochemistry **29**(37): 8509-8517; Ngo *et al.* (2 March 1995) "The Protein Folding Problem and Tertiary Structure Prediction, Chapter 14: Computational Complexity Protein Structure Prediction, and the Levinthal Paradox" pp. 492-495]. However, the specification provides little or no guidance beyond the mere presentation of sequence data to enable one of ordinary skill in the art to determine, without undue experimentation, the positions in the protein which are tolerant to change (e.g. such as by amino acid substitutions or deletions), and the nature and extent of changes that can be made in these positions.

Although the specification outlines art-recognized procedures for producing variants, this is not adequate guidance as to the nature of active variants that may be

constructed, but is merely an invitation to the artisan to use the current invention as a starting point for further experimentation. Even if an active or binding site were identified in the specification, it may not be sufficient, as the ordinary artisan would immediately recognize that an active or binding site must assume the proper three-dimensional configuration to be active, which conformation is dependent upon surrounding residues; therefore substitution of non-essential residues can often destroy activity. The art recognizes that function cannot be predicted from structure alone [Bork (2000) "Powers and Pitfalls in Sequence Analysis: The 70% Hurdle." Genome Research **10**:398-400; Skolnick and Fetrow (2000) "From gene to protein structure and function: novel applications of computational approaches in the genomic era." Trends in Biotech. **18**(1): 34-39; Doerks *et al*. (June 1998) "Protein annotation: detective work for function prediction." Trends in Genetics **14**(6): 248-250; Smith and Zhang (November 1997) "The challenges of genome sequence annotation or 'The devil is in the details'." Nature Biotechnology **15**:1222-1223; Brenner (April 1999) "Errors in genome annotation." Trends in Genetics **15**(4): 132-133; Bork and Bairoch (October 1996) "Go hunting in sequence databases but watch out for the traps." Trends in Genetics **12**(10): 425-427].

Due to the large quantity of experimentation necessary to generate the large number of variants recited in the claims and screen same for activity, the lack of direction/guidance presented in the specification regarding which structural features are required in order to provide activity, the absence of working examples directed to same, the complex nature of the invention, the state of the prior art which establishes the unpredictability of the effects of mutation on protein structure and function, and the breadth of the claims which fail to recite any structural or functional limitations, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

(2) The claims encompass methods of screening using transgenic animals. Dependent claim 14 specifically recites use of "cells containing a G protein-coupled receptor protein comprising … SEQ ID NO: 1". Furthermore, the specification specifically envisions use of transgenic animals (starting at ¶380).

However, there are no methods or working examples disclosed in the instant application whereby a multicellular animal with the incorporated claimed gene is demonstrated to express the encoded peptide or knockout. The unpredictability of the art is *very high* with regards to making transgenic animals other than mice. For example, Wang et al. (Nuc. Acids Res. 27: 4609-4618, 1999; pg 4617) surveyed gene expression in transgenic animals and found in each experimental animal with a single "knock-in" gene, multiple changes in genes and protein products, often many of which were unrelated to the original gene. Likewise, Kaufman et al (Blood 94: 3178-3184, 1999) found transgene expression levels in their transfected animals varied from "full" (9 %) to "intermediate" to "none" due to factors such as "vector poisoning" and spontaneous structural rearrangements (pg 3180, col 1, 2nd full paragraph; pg 3182-3183). Based on the art recognized unpredictability of isolating and using embryonic stem cells or other embryonal cells from animals other than mice to produce transgenic animals, and in view of the lack of guidance provided by the specification for identifying and isolating embryonal cells that can contribute to the germ line of any non-human mammal other than the mouse, such as dogs or cows, the skilled artisan would not have had a reasonable expectation of success in generating any and all non-human transgenic animals using ES cell technology.

(3) While the specification enables the skilled artisan to use the claimed method to identify modulators of the interaction between fatty acids and the protein of SEQ ID NO: 1, the specification does not enable the skilled artisan to use the claimed method "for confirming" "a drug for preventing/treating diabetes mellitus" as recited in claims 67, 68 and 70. The specification does not provide any examples indicating that regulation of the activity of SEQ ID NO: 1 induced by fatty acids can be used to prevent or treat diabetes. The specification does not teach any correspondence between the activity of SEQ ID NO: 1 and diabetes. The specification does not teach whether an agonist or antagonist of SEQ ID NO: 1 would be used to treat diabetes. Instead, the specification merely recites a long list of diseases for which modulators of SEQ ID NO: 1 can be used for treatment (these recited in claim 67). The specification's general discussion of treating a vast genus of diseases constitutes and invitation to experiment by trial and

error. At the time of filing of the instant application, significant experimentation would be required to determine if administration of said modulators could be used to prevent or treat diabetes.

Claim Rejections - 35 USC § 112, 1st paragraph, written description

Claims 1, 3, 14, 67, 68 and 70 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are genus claims because the claims are directed to compositions and cells comprising variant polypeptides. As described above, in the section titled, "Claim Rejections - 35 U.S.C. 112, 1st Paragraph, enablement" the genus of polypeptides encompassed by the claims is highly variant because a significant number of structural differences between genus members are permitted. The claims do not require that the polypeptides possess any particular conserved structure or function, or other disclosed distinguishing feature. The claims only require using "the same or substantially the same amino acid sequence as the amino acid sequence represented by SEQ ID NO: 1" or "its partial peptide". Thus, the claims are drawn to a genus of polypeptides defined only by sequence similarity. However, the instant specification fails to describe the entire genus of polypeptides that are encompassed by each of these claims. From the specification, it is clear that Applicants has possession of a receptor comprising SEQ ID NO: 1. The specification fails to describe or teach any other polypeptides which differs from SEQ ID NO: 1 and that retains the characteristics of the parent polypeptides.

The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant identifying characteristics, i.e. structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between structure and function, or by a

combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. In the instant case, the specification fails to provide sufficient descriptive information, such as definitive structural or functional features, or critical conserved regions, of the genus of polypeptides. There is not even identification of any particular portion of the structure that must be conserved. Structural features that could distinguish encoded polypeptides in the genus from others in the protein class are missing from the disclosure. The specification and claims do not provide any description of what changes should be made. There is no description of the sites at which variability may be tolerated and there is no information regarding the relation of structure to function. The general knowledge and level of skill in the art do not supplement the omitted description because specific, not general, guidance is what is needed. Furthermore, the prior art does not provide compensatory structural or correlative teachings sufficient to enable one of skill to isolate and identify the polypeptides encompassed. Thus, no identifying characteristics or properties of the instant polypeptides are provided such that one of skill would be able to predictably identify the encompassed molecules as being identical to those instantly claimed. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, Applicants were not in possession of the claimed genus.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed" (pg 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed" (pg 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of polypeptides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written

description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016. One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGFs were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only methods of screening, or confirming that a drug binds to a receptor that comprise contacting a polypeptide comprising SEQ ID NO: 1 with a test compound and a fatty acid, and determining the effect of the test compound on the binding or cell-based activities induced by the fatty acid binding the receptor, but not the full breadth of the claim meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (pg 1115).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 3, 14, 67, 68 and 70 are rejected under 35 U.S.C. 102(b) as being anticipated by Sidhu et al, 2000. Journal of Physiology. 528(1): 165-176.

The recitation that the method of screening is one "that changes the binding property of a G protein coupled receptor … to a fatty acid or salt thereof" in the preamble of claim 1 is interpreted as an intended use and bears no accorded patentable weight to distinguish the claimed method over one from the prior art. A preamble is generally not accorded any patentable weight where it merely recites the purpose of a process, and where the body of the claim does not depend on the preamble for completeness but, instead, the process steps are able to stand alone. See *In re Hirao*, 535 F.2d 67, 190 USPQ 15 (CCPA 1976) and *Kropa v. Robie*, 187 F.2d 150, 152, 88

USPQ 478, 481 (CCPA 1951). Thus, claim 1 encompasses any method of screening that comprises using a G-protein coupled receptor of SEQ ID NO: 1 or "a substantially the same amino acid sequence" and a fatty acid. The sequence of SEQ ID NO: 1 is 100% identical with a GPCR known in the art as human GPR120 (see the record for GenBank Protein Database Accession Number AAIOO1176, titled "GPR120 protein [Home sapiens]", dated Oct 4, 2006, 1 page as printed; cited here solely as evidence of the amino acid sequence of GPR120).

The method of claim 1 encompasses methods of screening using a G-protein coupled receptor of SEQ ID NO: 1 that is endogenously expressed in a cell. Sidhu et al teaches that "the application of dodecanoic acid (C12), in the absence of albumin, onto the CCK-secreting enteroendocrine cell line STIC-1 directly stimulates CCK [cholecystokinin] secretion". Dodecanoic acid is a fatty acid, and "elevates $[Ca^{2+}]_i$ when applied to STIC-1" (pg 168). The STC-1 cells used by Sidhu et al inherently express a G-protein coupled receptor of SEQ ID NO: 1 (human GPR120) and this receptor mediates the cholecystokinin secretion and increase in intracellular calcium induced by free fatty acids, as evidenced by Tanaka et al (2008. Naunyn-Schmiedeberg's Arch Pharmacol. 377:523-527; cited here solely to provide evidence of inherency). Therefore, Sidhu et al teach a method of screening that comprises using a G-protein coupled receptor of SEQ ID NO: 1 (GPR120) and a fatty acid (dodecanoic acid). Therefore, the teachings of Sidhu et al anticipate claim 1.

Claim 3 depends from claim 1. The recitation that the method of claim 3 is "for screening an agonist or an antagonist to a G protein coupled receptor" in the preamble of claim 3 is interpreted as an intended use and bears no accorded patentable weight to distinguish the claimed method over one from the prior art, for the same reasons as for claim 1. Thus, claim 3 encompasses any method of screening that comprises using a G-protein coupled receptor of SEQ ID NO: 1 or "a substantially the same amino acid sequence" and a "compound that changes the binding property of the receptor protein … to a fatty acid". The claim also requires use of a fatty acid, because this is required by parent claim 1. Sidhu et al further teach that "[i]n our experimental system, fatty acids were unable to elicit a rise in $[Ca^{2+}]_i$ in the presence of BSA" (pg 168). Thus, BSA is a

compound that changes the binding property of the fatty acid to its receptor. Therefore, the teachings of Sidhu et al also anticipate claim 3.

Claim 14 depends from claim 1. The recitation that the method of claim 14 is "for screening an agonist a G protein coupled receptor" in the preamble of claim 14 is interpreted as an intended use and bears no accorded patentable weight to distinguish the claimed method over one from the prior art, for the same reasons as for claim 1. Thus, claim 14 encompasses any method of screening that comprises assaying "the intracellular Ca^{2+} level increasing activity" when a test compound is contacted with cells containing a GPCR of SEQ ID NO: 1. The teachings of Sidhu et al described above anticipate claim 14 for the same reasons as for claim 1 (dodecanoic acid is encompassed by the recited "test compound" recited in claim 14).

Claim 67 is an independent claim reciting a method for confirming that a drug for preventing/treating diabetes mellitus (the elected species of disease) binds to a G-PCR comprising SEQ ID NO: 1 which comprises using the receptor protein in an assay. The recitation that the method is "for confirming that … a drug for preventing/treating diabetes mellitus … binds to a G protein-coupled receptor" is interpreted as an intended use and bears no accorded patentable weight to distinguish the claimed method over one from the prior art, for the same reasons as for claim 1. Therefore, claim 67 encompasses any method of using a receptor of SEQ ID NO: 1 "in an assay". As such, the teachings of Sidhu et al described above anticipate claim 67 for the same reasons as for claim 1.

Claim 68 depends from claim 67. The recitation that the method is "for confirmation that a drug for preventing/treating diabetes mellitus … is an agonist to a G protein-coupled receptor" is interpreted as an intended use and bears no accorded patentable weight to distinguish the claimed method over one from the prior art, for the same reasons as for claim 1. Therefore, claim 68 encompasses any method of using a receptor of SEQ ID NO: 1 "in an assay". As such, the teachings of Sidhu et al described above anticipate claim 68 for the same reasons as for claim 1.

Claim 70 depends from claim 70 and recites that the "binding amount of each drug to the receptor protein" is "determined when each drug is contacted with the

receptor protein". In the teachings of Sidhu et al described above, the receptor (expressed by the STIC-1 cells) is contacted with the fatty acid (dodecanoic acid), and the binding amount is determined by measuring the increase in intracellular calcium concentration. As such, the teachings of Sidhu et al described above anticipate claim 70 for the same reasons as for claim 1.

Conclusion

No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zachary C. Howard whose telephone number is 571-272-2877. The examiner can normally be reached on M-F 9:30 AM - 6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary B. Nickol can be reached on 571-272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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